REMARKS/ARGUMENTS

Claims 1-8, 32-37, and 43 are currently pending. Herein claims 1, 4, 32, 35 and 38 are amended for clarification and claims 37 and 51-53 are cancelled, all without prejudice and without acquiescence. No new matter is entered herein. Applicants reserve the right to pursue cancelled material in future prosecution.

Claims 1-8, 32-39, 43, and 50-51 are rejected under 35 U.S.C. §112, first paragraph because the specification allegedly does not reasonably provide enablement for methods of detecting any NF-κB related medical condition in any organism. Applicants respectfully disagree, but amend the claims herein without prejudice and without acquiescence to further the prosecution of this case.

Applicants submit herewith a Supplemental IDS entering all of the references cited herein.

The Examiner indicates in the outstanding Office Action that Applicants would need to narrow the claim scope to mutations in human NEMO for Incontinentia pigmenti that are only in regions having already known disease-causing mutations. Applicants reiterate that this is an inappropriate request given the nature of the invention and the disclosure provided in the specification. The presently pending claims are directed to identifying any mutation in human NEMO, regardless of their location in the gene. One of skill in the art, and particularly in an art traditionally having high skill such as molecular biology, would be able to identify mutations in any part of SEQ ID NO:1, *such as in exactly the same manner that they have identified the known mutations*! Why does the Office discriminate between regions of the genomic DNA as being differentially enabled when Applicants have already demonstrated the ability to identify disease-causing mutations in multiple different regions (exons, introns, stop codons, *etc.*) of SEQ ID NO:1? In the presently pending claims, Applicants are claiming identifying an alteration in any region *so long as it resides in SEQ ID NO:1*, and therefore one of skill in the art knows exactly how to make and use the invention having such a focused field with which to work and pursuant to methods taught in the application and known at the time of filing.

As Applicants noted in the previous Response and exemplary references submitted

therewith, which was apparently not made clear to the Examiner, it is known that there are disease-causing mutations in non-coding sequences. Applicants did not submit these references for demonstration for the disease of Incontinentia pigmenti, but rather to illustrate that disease-causing mutations can exist in non-exon regions of a gene. Applicants submit herewith in a Supplemental IDS additional references available at the time of filing to demonstrate that mutations can exist in non-coding sequences, such as introns (Janssen et al., 2000; Flagiello et al., 1998; Hobson et al., 2000; Pyne et al., 2000) and untranslated regions (UTRs) (Harland et al., 2000; Ionasescu et al. (1996)). Therefore, given that the knowledge to search for mutations in non-coding sequences existed and the mechanism(s) to identify them was known and was demonstrated by Applicants themselves, Applicants strongly assert that the instant specification is enabled. Moreover, Applicants reiterate that the mechanics of the exemplary and very routine methods (PCR and electrophoresis, for example) for identifying mutations do not discriminate between a 5′ UTR or an exon, for example.

The Examiner states on Page 3, "[Applicant]...does not reasonably provide enablement for methods of detecting IP in a human by analyzing a sample for an alteration in a regulatory nucleic acid, a promoter nucleic acid, the 5′ untranslated region, or the 3′ untranslated region of the nucleic acid sequence of SEQ ID NO:1. This is inaccurate. At the very least, and as stated in the specification on Page 53, lines 22-23, and in Fig. 3E, the large deletion begins in intron 3 but ends far after the last exon, exon 10. Therefore, the deletion removes the 3′ UTR region. Thus, Applicants *have* demonstrated an alteration in an untranslated region.

Applicants amend herein the claims to remove the term "promoter nucleic acid" without prejudice and without acquiescence, to further the prosecution of this case. Applicants reserve the right to pursue this matter in future prosecution. Applicants retain the term "regulatory region", however, given that regulatory regions were known at the time of filing to be in introns (Shamsher et al., 2000) and UTRs (see above). Furthermore, the afore-mentioned mutation removing from intron 3 to well past exon 10 would remove the poly(A) signal, and as indicated in Xu et al. (2001), Graber et al. (1999), McQueen et al. (2001), and Rothnie et al. (2001), poly(A) signals are considered in the art to be regulatory.

Thus, in view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is

respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

Applicants believe no fee is due with this response except for the fee for the Supplemental IDS. However, if another fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P01961US1 from which the undersigned is authorized to draw.

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Respectfully submitted,

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